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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/822,033	03/24/97	MARASCO	W 43471-FWC

EXAMINER
BRUNOVSKIS,P

ART UNIT	PAPER NUMBER
1632	17

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DATE MAILED: 02/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
08/822,033	Marasco et al.
Examiner	**Group Art Unit**
Peter Brunovskis	1632

☒ Responsive to communication(s) filed on *Jan 18, 2001*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1 and 3-16* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 3-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Continued Prosecution Application

The request filed on January 18, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/822,033 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5 and 7-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Beug et al. in view of Chaudhary et al. and Wu et al. Beug et al. disclose a nucleic acid carrier, which is a fusion protein consisting of transferrin fused to a polycationic polypeptide, complexed with a nucleic acid molecule. Beug et al. also suggest the use of protamine as the nucleic acid binding moiety (p. 6) and demonstrate the use of the carrier to transform cells *in vitro* (examples 5-13). Beug et al. do not teach a carrier in which the targeting moiety is an antibody or the nucleic acid encodes *Pseudomonas* exotoxin A (PEA), nor do they demonstrate transformation of cells *in vivo*. Chaudhary et al. disclose a fusion protein which consists of a single chain antibody having a truncated form of PEA (containing domain III) fused to its carboxyl end (p. 1068). This fusion protein is used to deliver PEA specifically to cells expressing the surface antigen recognized by the antibody (entire document). Chaudhary et al. teach a method for cloning antibody genes (entire document), and a method for producing and purifying the fusion protein

(p. 1067). Chaudhary et al. teach that the truncated form of PEA is a potent toxin and disclose a plasmid encoding the truncated PEA (p. 1066, Fig. 5). Chaudhary et al. teach that a fusion protein containing an antibody against the interleukin-2 receptor was used to selectively deliver PEA to cells expressing the receptor (p. 1066). Wu et al. teach a nucleic acid carrier consisting of a cell-receptor specific ligand linked to a polycationic polypeptide (entire document), and demonstrate successful use of this carrier to deliver and express DNA to a specific cell type *in vivo* (by intravenous injection; col. 11). Wu et al. suggest that an antibody could be used as targeting moiety (col. 6, lines 3-7), that protamine could be used as the polycationic polypeptide (col. 4, lines 39-44), and that a peptide bond could be used to link the targeting and DNA binding moieties (col. 5, lines 45-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the prior art to develop the claimed compositions and methods. It would have been obvious to modify the transferrin-polycationic polypeptide fusion of Beug et al. by substituting an antibody for transferrin, given the suggestion of Wu et al. to use an antibody for cell type-specific targeting of DNA and the demonstration of successful cell type targeting with antibodies by Chaudhary et al. It would have been obvious to use protamine as the DNA binding protein, given the suggestion to do so by Beug et al. and Wu et al. It would have been obvious to fuse the DNA binding protein to the carboxyl end of the antibody, since Chaudhary et al. had shown that this arrangement preserved the ability of the antibody to recognize antigen. Having made the antibody-polycationic polypeptide fusion protein by the methods of Chaudhary et al., it would have been obvious to use it to deliver polynucleotides *in vivo* as discussed by Beug et al. and demonstrated by Wu et al. using different targeting moieties. It would have been obvious to deliver a gene encoding PEA, since Chaudhary et al. had shown this toxin to be extremely potent. One would have been motivated to develop the claimed compositions and methods, given the knowledge that virtually any nucleic acid could be delivered in this manner, as taught by Beug et al., and that use of antibodies would allow targeting of any cell type which

produces a cell type-specific antigen. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 6 is rejected under 35 U.S.C. § 103 as being unpatentable over Beug et al. in view of Chaudhary et al. and Wu et al. as applied to claims 1, 3-5 and 7-16 above, and further in view of Ryder et al. Beug et al. in view of Chaudhary et al. and Wu et al. teach fusion proteins, consisting of an antibody fused to a DNA-binding protein, complexed with nucleic acids, as discussed above. Beug et al. in view of Chaudhary et al. and Wu et al. do not teach fusion proteins wherein the DNA-binding protein is one of those recited in claim 6. Ryder et al. disclose the amino acid sequences of the DNA-binding regions of three *jun* proteins (Fig. 2) and the nucleotide sequence of *jun-D* cDNA (Fig. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize one of the *jun* sequences disclosed by Ryder et al. as the DNA-binding moiety of the fusion protein of Beug et al. in view of Chaudhary et al. and Wu et al. One would have expected the *jun* protein to be effective, since it was known to bind certain DNA sequences. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.

Patent Examiner

Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER